Attorney Docket No.: 3745.234-US
Serial No.: 09/754,723
Filed: January 4, 2001
Inventor: Ole Kirk
Title: Use of A Peptide
Via Facsimile No.: 571-273-8300

REMARKS

I. Claim status. Claims 15-32 are pending. Claims 15 and 21-24 have been amended. Support for the amended claim is found in the originally filed claims and throughout the specification, e.g., at page 4, line 20 through page 7, line 19. By this Amendment, no new matter has been added to the application.

II. Claim rejections. The rejections set forth in the Final Office Action that was mailed on September 8, 2004 are summarized and addressed as follows.

(i) Rejections Under 35 U.S.C. §112, first paragraph (written description). Claims 22 and 30-32 have been rejected for allegedly failing to comply with the written description requirement. In response, without conceding the validity of the rejection, independent claim 22 has been amended. Claim 22 now calls for an insulinotropic GLP-1 related peptide selected from the group consisting of GLP-1 (7-37), GLP-1 (7-36) amide, an analogue of GLP-1 (7-37), an analogue of GLP-1 (7-36) amide, a functional derivative of GLP-1 (7-37), a functional derivative of GLP-1 (7-36) amide, a functional derivative of an analogue of GLP-1 (7-37) and a functional derivative of an analogue of GLP-1 (7-36) amide. Claims 30-32 depend from claim 22 and likewise call for an insulinotropic peptide selected from the same group.

Support for the amended claims is found in the specification at, e.g., page 4, line 20 through page 7, line 19. The present rejection should be withdrawn, accordingly.

(ii) Rejections Under 35 U.S.C. §112, second paragraph. Claims 15-20, 21, and 23-27 have been rejected for alleged indefiniteness. In response, without conceding the validity of the rejections, claims 15, 21 and 22-24 have been amended. The respective insulinotropic peptides called for in each claim are set forth in proper Markush format. The rejection should therefore be withdrawn.

(iii) Rejection Under 35 U.S.C. §103(a). Claims 15-32 have been rejected as obvious over Buckley et al., WO 91/11457 ("Buckley") in view of Gutniak et al., Diabetologia,

33(suppl.):A73, Abstract 246, 1990, Ramachandran et al., Diabete Metabolisme, 1(2):140-141, 1987; Del Prato et al., American J. of Med., 90(Suppl. 6A):6A-77S, 1991; and Parker et al., Diabetes, Vol 40, Suppl. 1, Abstract 847. The rejection is respectfully traversed, because the Examiner has relied on the instant specification for the motivation to combine the cited prior art to arrive at the claimed invention.

Both the motivation to combine the relevant elements and the suggestion of success must be found in the prior art to satisfy the requirements for maintaining an obviousness rejection. *In re The Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988) ("[b]oth the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure"). The mere mention of elements in different references is not sufficient motivation to combine them to arrive at a claimed invention. *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998) ("[T]he examiner must show reasons that the skilled artisan, *confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.*") (citations omitted, emphasis added).

Buckley, the primary reference relied upon by the Examiner, discloses GLP 1 peptides for treatment of diabetes. Buckley fails to disclose metformin or any other oral hypoglycemic. Gutniak stands merely for the proposition that GLP-1(7-36) stimulates insulin secretion in vivo. Parker discloses only GLP-1(7-37) and glibenclamide (not metformin). Ramachandran discloses only glibenclamide plus metformin to treat immunogenic insulin resistance (IRR). Del Prato discloses only that improvement in insulin secretion and perhaps insulin sensitivity appears to be responsible for the beneficial effect of sulfonylureas on glucose metabolism.

The instant claims call for treating type 2 diabetes by administering an effective amount of metformin in combination with one of certain insulinotropic GLP-1 peptides. The

Examiner recognizes the primary reference fails to disclose or suggest the claimed combination treatment. The Examiner attempts to cure this defect by finding strained motivations to pick and choose among particular elements found in the secondary references.

The Examiner, for instance, states that "Parker et al[.] broadly teaches the combination of GLP-1 peptides and oral hypoglycemic agents to increase insulin secretion." Office Action dated December 12, 2003 at page 5. This general statement is too broad to provide any motivation to combine GLP-1 peptides and metformin. Moreover, metformin does not increase insulin secretion but, rather, sensitizes cells to insulin action, thereby lowering insulin secretion. Moreover, as noted by the Examiner, del Prato teaches that diabetes is a complicated disease. Accordingly, at the time the invention was made, one of ordinary skill in the art could not predict that all oral hypoglycemics would be alike. At the time the invention was made, a general teaching about oral hypoglycemics without any further direction on how to proceed would not point to combining a GLP-1 peptide with metformin.

The Examiner also uses a strained interpretation of Ramachandran for motivation to arrive at the claimed invention. The Examiner cites Ramachandran for "the combination of glibenclamide and metformin for the treatment of Type 2 diabetes." Final Office Action at page 5. Ramachandran, however, provides no motivation to administer metformin with a GLP-1 peptide. First, the study reported in Ramachandran was not controlled. Accordingly, a conclusion that the results reported in Ramachandran are due to the reported treatment is not credible. Moreover, Ramachandran used the combination of glibenclamide and metformin to treat patients who have developed immunogenic insulin resistance. The Examiner has cited no authority for the expectation that agents developed to alleviate immunogenic insulin resistance could be used successfully to treat Type 2 diabetes, as called for in the claims. Additionally, combining the primary reference, Buckley, with Ramachandran requires first modifying Ramachandran by removing glibenclamide from the glibenclamide-metformin combination.

There is no suggestion in the prior art to do so. Finally, Ramachandran states explicitly that "[t]he present study suggests that a trial of oral hypoglycemic agents may be worthwhile in *selected NIDDM patients who show immunogenic insulin resistance*." (emphasis added) Thus, Ramachandran acknowledges that the reported findings suggest further treatments that are limited in scope. Accordingly, Ramachandran does not provide the required motivation or the required suggestion of success to arrive at the instant claims.

The Examiner attempts to make up for the lack of a specific suggestion to arrive at the claimed invention by stating that the claimed combination is not obvious to try, but is rather "common sense." Final Office Action at page 5. At the time the invention was made, however, it was not "common sense" to combine GLP-1 and metformin for treatment of Type 2 diabetes. The prior art cited by the Examiner does not disclose or suggest any combination of GLP-1 and metformin. It is therefore not "common sense" to modify the prior art to arrive at the present claims. The rejections for obviousness should therefore be withdrawn.

For at least the reasons given above, claims 15-20 and 21-32 are not obvious over the prior art of record. Reconsideration of these claims and withdrawal of the rejection under 35 U.S.C. § 103(a) is requested.

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CONCLUSION

This application is believed to be in condition for allowance, which is earnestly solicited.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

Date: October 3, 2005

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